

## Conduction system defects in three perinatal patients with arrhythmia

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**SUMMARY** The cardiac conduction systems of three patients who died in the perinatal period were studied histologically. Rhythm disturbances were observed in these patients immediately before death. The sinus node was notably hypoplastic without increase in fibrous content in all cases. The atrioventricular node was smaller than expected in all, and the entire atrioventricular conduction axis was small in two cases. This study supports the need for a detailed examination of the cardiac conduction system so as to provide a better understanding of the clinicoanatomical relation in the context of fatal perinatal arrhythmias.

Although the electrophysiological mechanisms of cardiac arrhythmias are well known, very little is known about the structure of the sinus node and atrioventricular conduction system in these circumstances. This is mostly due to the fact that few neonates with conduction disturbances recorded during life have detailed examination of their conduction system after death. Reports of the pathology of the neonatal sinus node are rare. In particular, discrete hypoplasia or underdevelopment of the sinus node is virtually unreported. To the best of our knowledge only one case of hypoplastic sinus node associated with atrial tachycardia has so far been described.<sup>1</sup> Recently, we studied the sinus node and atrioventricular conduction system of three hearts from perinatal patients who had cardiac arrhythmias immediately before death. At presentation, all three patients were thought to have cardiac abnormalities. In this report we consider the clinical significance of the unusual histological findings, especially of the sinus node, in the light of the clinical observations.

### Materials and method

The hearts from three perinatal patients with documented conduction disorders were removed at

necropsy and fixed in formol saline. Three blocks of tissue were removed from each heart. The first block consisted of the entire junction of the right atrium with the superior caval vein. The orifice of the caval vein was preserved by filling it with a bolus of tissue paper. The second block consisted of the inferior part of the interatrial septum and superior portion of the interventricular septum. The third block comprised the remaining atrioventricular junction. These tissue blocks were processed by the method detailed by Smith *et al.*<sup>2</sup> The tissue paper plug was removed from the first block just before embedding in Fibrowax. Serial sections of 10 µm thickness were cut from each block, and all sections were collected. The first block was sectioned in a plane which cut horizontally across the orifice of the caval vein. The second block was cut in a frontal plane relative to the cardiac septum. The third block was sectioned in planes which profiled the atrioventricular junction. Every twenty fifth section was mounted and stained with a modified Masson's trichrome technique. Further sections were stained where necessary.

### CLINICAL DETAILS

#### Case 1

The mother was admitted for hospital observation because her pregnancy was "large for dates" and showed hydramnios. The fetus was noted to have episodes of supraventricular tachycardia and heart rates up to 300 beats/min. The fetal arrhythmia did

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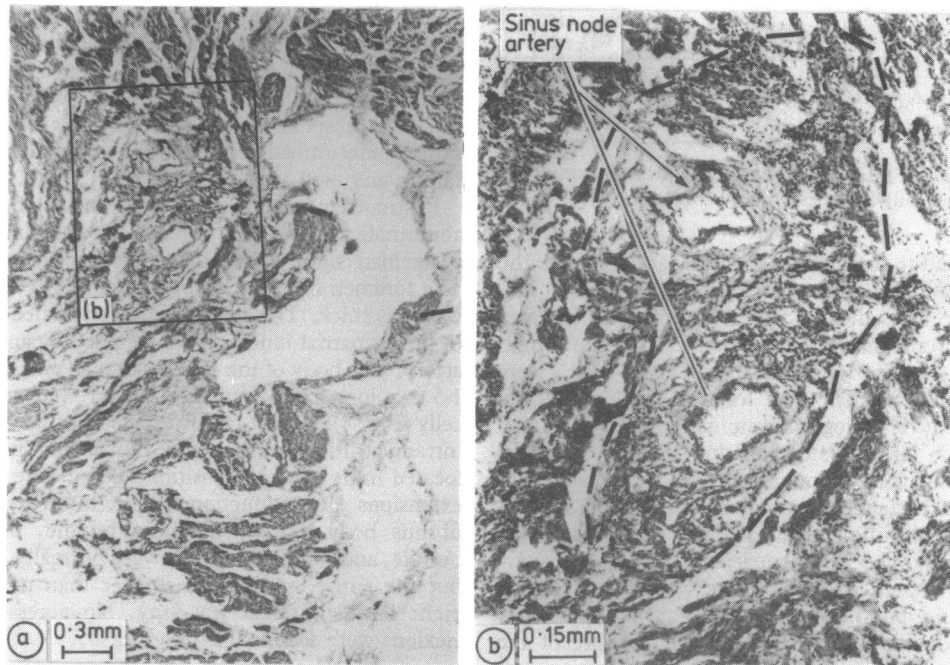


Fig. 1 Histological appearance of hypoplastic sinus node (case 1) (a) and magnified in (b) to show the few nodal cells surrounding the nodal artery. The extent of the node is marked by broken lines in (b).

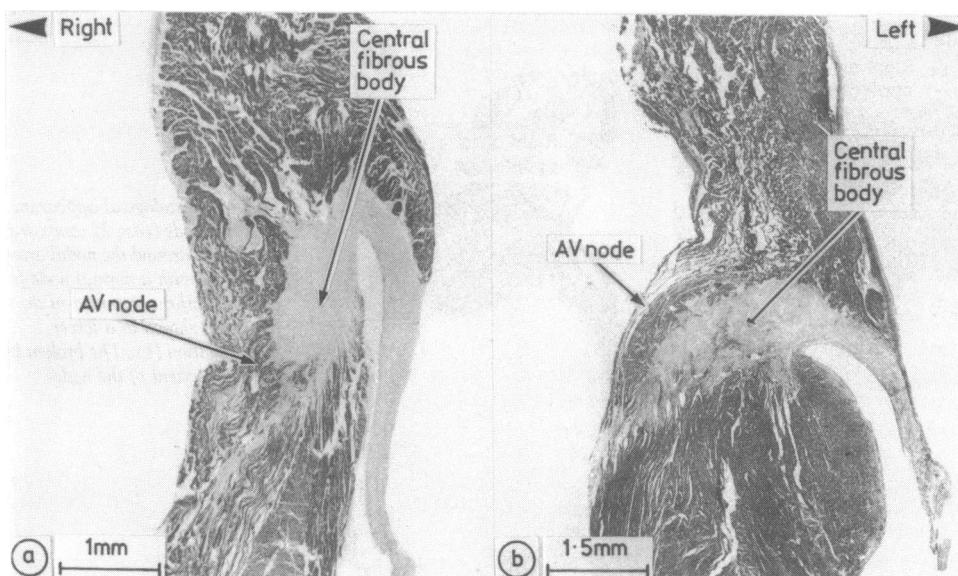


Fig. 2 Histological appearance of atrioventricular junction in the plane of the atrioventricular (AV) node. The hypoplastic node from the patient in case 1 (a) is compared with that from the normal heart (b) of a 2 day old infant.

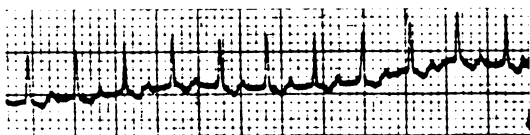


Fig. 3 Lead II trace of electrocardiogram from the patient in case 2 showing supraventricular tachycardia.

not respond to the digoxin and verapamil given to the mother. While under observation at 32 weeks' gestation the fetus died in utero. Labour was induced and a hydropic male fetus was delivered by the vertex. On gross examination the heart and great vessels were anatomically normal. The foramen ovale and duct were patent. Histological examination showed a small sinus node located lateral to the superior cavoatrial junction. It was very poorly formed and consisted of only a few nodal cells around a nodal artery (Fig. 1). Its maximum dimensions were 1.1 mm wide and 2 mm long. The atrioventricular node was grossly underdeveloped, although there was a well formed bundle and bundle branches (Fig. 2). Only a few nodal and transitional cells marked the site of the node. The remaining atrioventricular junction was normal.

#### Case 2

The mother was induced at 34 weeks' gestation for

fetal ascites and supraventricular tachycardia. The infant, a boy, developed heart failure with continuing severe ascites and tachycardia (Fig. 3). Cardiac catheterisation showed poor right ventricular function. He responded temporarily to treatment but rapidly succumbed to progressive intractable cardiac failure and died at the age of 3 days.

Postmortem examination of the heart showed no abnormality except the presence of a prominent post-eustachian sinus at the inferior cavoatrial junction. The foramen ovale was probe patent, and the ductal wall was thick. The sinus node was situated laterally in the cavoatrial junction and supplied by an anterior artery. The body of the node was small and measured 1.5 mm long and 1 mm wide. There were few nodal cells (Fig. 4). A thin tail of the node could be traced intramyocardially. The atrioventricular node was located in its expected position. There were multiple extensions of conduction tissue into the central fibrous body. The penetrating bundle, branching bundle, and bundle branches were normally situated, but the entire system was smaller than usual. The right bundle branch was tiny. No accessory connexions were seen.

#### Case 3

A baby was born at term after a normal pregnancy. He gasped initially but did not develop adequate respirations. His electrocardiogram showed a very

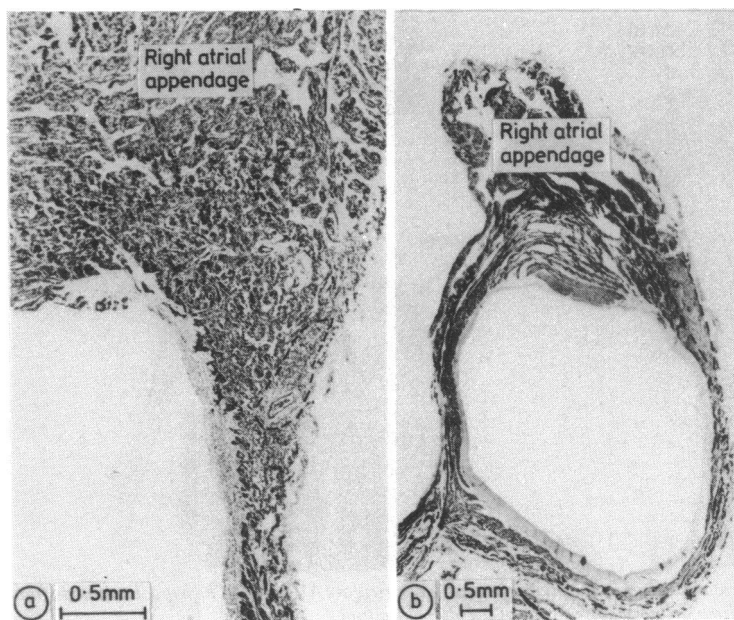


Fig. 4 Histological appearance of the sinus node (case 2) composed of a small area around the nodal artery (a) compared with a normal node from a newborn infant sectioned in the same plane but shown at a lower magnification (b). The broken lines mark the extent of the nodes.

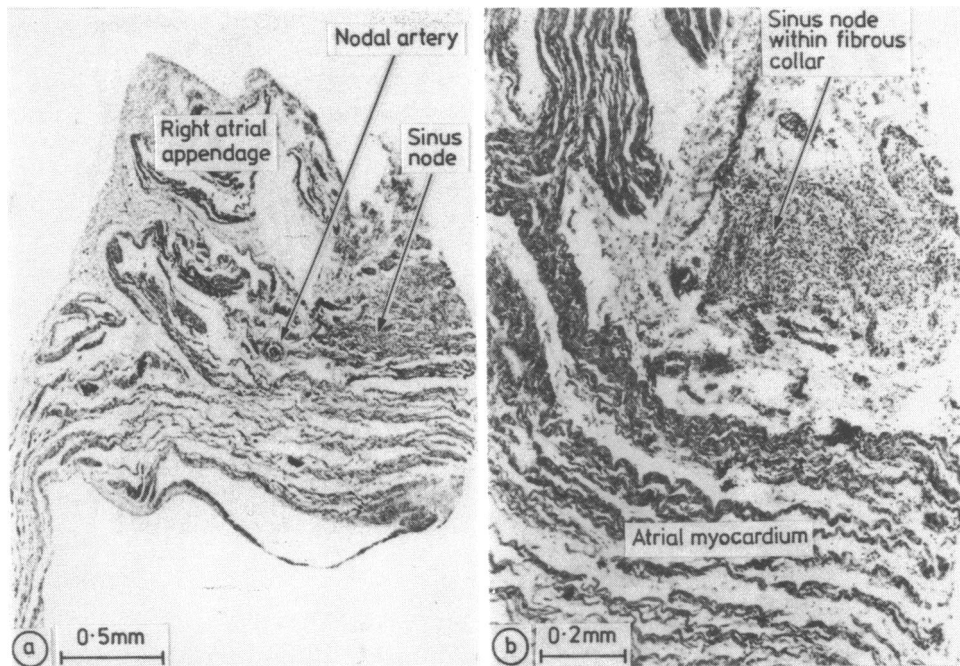


Fig. 5 Histological appearance of the right cavoatrial junction (case 3) (a) showing the nodal artery which courses within the transitional cells of the node. Another section, inferior to (a), at higher magnification shows the fibrous tissue around the node (b).

variable rhythm consisting of episodes of supraventricular extrasystoles with intervening periods of bradycardia. Congenital heart disease was suspected. The baby died aged 1½ hours despite continuous and appropriate resuscitative measures.

No anatomical abnormalities were noted in the heart, great arteries, or veins at necropsy. The foramen ovale and duct were patent. Histological examination showed a grossly abnormal cardiac conduction system. The sinus node was tiny and located just to the right of the crest of the right atrial appendage. The body of the node measured no more than 0.6 mm long and 0.2 mm wide. It had no direct arterial supply and was insulated in most parts by fibrous tissue from the rest of the atrial myocardium. The sinus node artery skimmed the superior region of transitional cells (Fig. 5). The atrioventricular system was normally distributed proximally but was much smaller than expected. The origins of the bundle branches were tenuous. Anteriorly, a tiny accessory bundle, 12 µm thick and comprising of a few myocardial cells, connected the branching bundle to the left bundle branch (Fig. 6). Examination of the parietal atrioventricular junctional area did not show any further accessory connexions.

## Discussion

Arrhythmias in childhood are usually too benign to cause symptoms or too transient to be identified. There is, however, a very small group of children in whom these disturbances in rhythm are persistent and can and do prove fatal. We have recently made a histological examination of the conduction system in three patients in whom the arrhythmias were observed immediately before death. In all three cases there were no gross anatomical abnormalities of the heart which might have potentiated malformations of the conduction system. This absence of anatomical malformation was particularly surprising in the neonate in case 3, in whom the clinical signs suggested "congenital heart disease."

The normal sinus node, unlike that seen in older individuals,<sup>3,4</sup> does not have a strong collagen network. It has been suggested that the collagen framework that separates the nodal cells into small clusters has a part in stabilising the electrical activity of the sinus node.<sup>5</sup> In infants, electrical instability may be partly due to poor formation of the nodal collagen.<sup>6</sup> In our three hearts there was a paucity of fibrous tissue within the sinus node, and the nodal

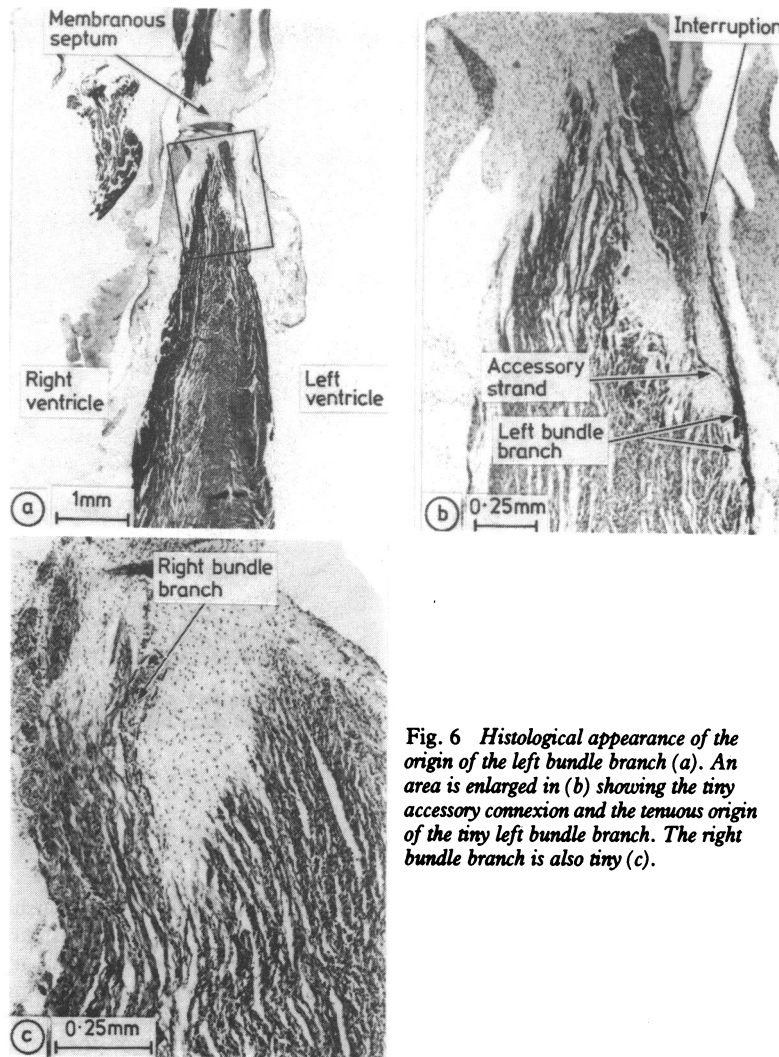


Fig. 6 Histological appearance of the origin of the left bundle branch (a). An area is enlarged in (b) showing the tiny accessory connexion and the tenuous origin of the tiny left bundle branch. The right bundle branch is also tiny (c).

cells were not well segregated into groups. More significantly, the sinus nodes in all our cases were notably hypoplastic and lacking in bulk. The dimensions were less than half the normal range for neonates<sup>7</sup> and smaller than for fetuses.<sup>8</sup>

Atrial arrhythmias have been associated with a loss in nodal fibres not accompanied by an increase in connective tissue.<sup>9</sup> The loss in nodal fibres in patients in this study, who ranged from a 2 year old to a patient in his ninth decade, was thought to be due to a degenerative process. In contrast, all our patients were in the perinatal age range. We therefore feel that the hypoplasia of the sinus node in our cases was due to an arrest or a defect in development rather than an

active degenerative process.

It seems probable that the sinus node defect could, in itself, have an effect on the heart rhythm. Nevertheless, on its own, this is unlikely to account for the fatal outcome. All our cases had additional poor formation of the atrioventricular conduction axis. In the two cases in which supraventricular tachycardia was noted the atrioventricular node was either hypoplastic or smaller than expected. In the other case, in which the rhythm was variable, the atrioventricular conduction system was also small. A tiny accessory connexion was found between the branching bundle and the left bundle branch. The "arrhythmogenic" potential of this type of bypass

tract has previously been suggested.<sup>10</sup> The accessory pathway is exceedingly small, and pathways of this size could possibly have been missed in other cases. Another unusual finding (case 3) was the presence of a fibrous collar around the sinus node (although there was minimal fibrous tissue within the node). The collar permitted only minimal contact of the node with the rest of the atrial myocardium.

In all these cases of arrhythmia we were able to find abnormalities in the conduction system. Nevertheless, at this stage it is not possible to conclude that the arrhythmias were due to the specific defects of the conduction system. There is a clear anatomical correlation with the electrocardiographic findings in ventricular pre-excitation.<sup>11 12</sup> Anatomical correlations with other forms of arrhythmia are exceedingly difficult, although the possibilities are considerable.<sup>13</sup> There is much that needs to be investigated further. For instance, to what extent does hypoplasia of the atrioventricular node influence the heart rate? Is underdevelopment of the cardiac conduction system a major cause of fatal perinatal (particularly supraventricular) tachycardia? We hope that this study will generate more interest and prompt a detailed examination of the cardiac conduction system in all patients with confirmed electrographic changes who subsequently come to necropsy. Only in this way, and by preparing suitable controls, will we be able to evaluate precisely the clinical significance of changes seen under the microscope which otherwise must comprise, at best, circumstantial evidence.

We thank our clinical colleagues for permission to report details of their patients.

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